IFW/ 1616

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Nobuhiko KANAZASHI et al.	Group Art Unit: 1616
Application No.: 10/550,724	Examiner: Not Yet Assigned
Filed: September 26, 2005	Attorney Docket No.: 7378/84428
Confirmation No.: 5995	Customer No.: 42798

Title: COMPOUND HAVING AFFINITY WITH CALCIFIED TISSUE

SUBMISSION OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

Commissioner for Patents
Customer Service Window
Randolph Building
401 Dulany Street
Alexandria, VA 22314

Sir:

Applicants submit herewith an English translation of the International Preliminary Examination Report (IPER) from the related PCT application. Please enter this paper in the application file. Favorable first action is respectfully solicited.

Respectfully submitted,

Date: **July 19, 2006**

Kendrew H. Colton
Registration No. 30,368

OFFICIAL CORRESPONDENCE TO
Customer No. 42798
FITCH, EVEN, TABIN & FLANNERY
1801 K Street, NW, Suite 401L
Washington, DC 20006-1201
Tel: (202) 419-7000
Fax: (202) 419-7007

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference IFP-683	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/JP2004/004019	International filing date *(day/month/year)* 24 March 2004 (24.03.2004)	Priority date *(day/month/year)* 26 March 2003 (26.03.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant NIHON MEDI-PHYSICS CO. LTD.		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 22 February 2006 (22.02.2006)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 740 14 35	Authorized officer Yoshiko Kuwahara Telephone No. +41 22 338 90 90

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

Translation

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

	Date of mailing *(day/month/year)*
Applicant's or agent's file reference IFP-683	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2004/004019	24.03.2004	26.03.2003

International Patent Classification (IPC) or both national classification and IPC

Applicant
NIHON MEDI-PHYSICS CO. LTD.

1. This opinion contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/JP Facsimile No.	Authorized officer Telephone No.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/004019

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in the international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/004019

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has:

   ☐ paid additional fees

   ☐ paid additional fees under protest

   ☐ not paid additional fees

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

The inventions of claims 1-45 and the inventions of claims 46 and 47 comprise two groups of inventions.

The special technical feature of claims 1-45 is a compound having affinity for calcified tissue represented by the formula $(AC)_a$–MC–$(LI)_b$ and a drug, diagnostic agent, etc., containing the same.

On the other hand, the special technical feature of claims 46 and 47 is a method for selectively modifying a terminal amino group by conducting a reaction synthesizing a carbamate using a terminally reduced amino oligosaccharide comprising one or more monosaccharides selected from a group consisting of glucosamine, mannosamine, and galactosamine.

As a result, this examination finds that no technical relationship involving one or more of the same or corresponding special technical features exists among these groups of inventions, and they do not constitute one group of inventions so linked as to form a single general inventive concept.

4. Consequently, this opinion has been established in respect of the following parts of the international application:

   ☒ all parts

   ☐ the parts relating to claims Nos. _____

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/004019

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	2, 4, 5, 8-17, 20, 22-30, 46, 47	YES
	Claims	1, 3, 6, 7, 18, 19, 21, 31-45	NO
Inventive step (IS)	Claims	46, 47	YES
	Claims	1-45	NO
Industrial applicability (IA)	Claims	1-47	YES
	Claims		NO

2. Citations and explanations:

Document 1: JP 2002-187948 A (Sumitomo Chemical Co., Ltd.) 5 July 2002
Document 2: WO 89/11877 A1 (NEORX CORPORATION) 14 December 1989
Document 3: JP 2001-114792 A (Nihon Medi-Physics Co., Ltd.) 24 April 2001
Document 4: JP 4-202197 A (Ihara Chemical Industry Co., Ltd.) 22 July 1992

<Claims 1, 3, 6, 7, 18, 19, 21, and 31-45>

Based on the description in document 3 cited in the international search report, the inventions of claims 1, 3, 6, 7, 18, 19, 21, and 31-45 lack novelty and an inventive step.

Document 3 describes bisphosphonic acid derivatives represented by Formulas (7)-(10), (12), (19), (23), and (27), etc., that are useful as the active ingredient in an agent for bone diagnosis and a drug for the treatment of bone disease, and these compounds contain within their molecule a ligand that can bond to an organic phosphonic acid and/or metal atom, and the residue of a compound having a plurality of functional groups such as a halogen, amide group, etc.

<Claims 1-45>

Based on the descriptions in documents 1-3 cited in the international search report, the inventions of claims 1-45 lack an inventive step.

Document 1 states that an amide compound wherein an amino oligosaccharide is modified by a polyamino polycarboxylic acid such as ethylenediamine tetraacetate, diethylenetriamine pentaacetate, 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetate, etc. (a ligand that can form a chelate with a metal atom), can be used as a diagnostic imaging agent by forming a complex with a radioactive or paramagnetic metal atom). On the other hand, documents 2 and 3 state that a compound having a ligand that can form a chelate with a metal atom and a bisphosphonic acid site within its molecule can be useful as an agent for bone diagnosis and a drug for the treatment of bone disease. This being the case, this examination finds that based on the information in documents 2 and 3 persons skilled in the art can make a substitution using bisphosphonic acid in the amide compound that is useful as a diagnostic agent described in document 1 to give it functionality as a drug to treat (bone) disease.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/004019

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The compound having affinity with calcified tissue represented by the formula $(AC)_a$–MC–$(LI)_b$ of claim 1 includes an extremely large number of compounds. However, only a very small portion of the compounds represented by that formula are fully disclosed in the sense of PCT Article 5 or fully supported by the specification in the sense of PCT Article 6.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of Box V.2:

In addition, the specification of this application merely discloses that when the compound represented by Formula VI-1 is used, a more rapid elimination from the urine and clearance from the blood than the commercial product MDP are provided, and this examination cannot verify that an advantageous effect equivalent to that specifically disclosed is provided when other typical compounds represented by the formula $(AC)_a$–MC–$(LI)_b$ are used. Therefore, this examination finds that the inventions of claims 1-45 do not provide a particularly outstanding effect that could not be predicted by persons skilled in the art from the inventions described in documents 1-3.

<Claims 46 and 47>

None of the documents cited in the international search report discloses the inventions of claims 46 and 47, and therefore these inventions are novel and involve an inventive step.

More specifically documents 1-4, which are recognized as the most relevant prior art documents, do not disclose a method for selectively modifying a terminal amino group by conducting a reaction synthesizing a carbamate using a terminally reduced amino oligosaccharide comprising one or more monosaccharides selected from a group consisting of glucosamine, mannosamine, and galactosamine, etc.